REMARKS

Claims 1-15 are pending in this application. Claims 1-15 were rejected under 35 U.S.C. §112, first paragraph.

By this amendment, claim 7 has been canceled and claims 1, 9 and 11 have been amended without prejudice or disclaimer of any previously claimed subject matter. Support for the amendments can be found, *inter alia*, throughout the specification and, for example, at page 33, lines 5-7, page 34, lines 1-5, and in claim 8 as originally filed.

The amendments are made solely to promote prosecution without prejudice or disclaimer of any previously claimed subject matter. With respect to all amendments and cancelled claims, Applicant has not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicant expressly reserves the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "**Version with markings to show changes made**".

Applicant has carefully considered the points raised in the Office Action and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

Information disclosure statement

Applicant respectfully notes that a partially initialed Form PTO-1449 was returned with the final Office Action. The Examiner initialed the entries listed under "Other Documents" but did not initial the U.S. or Foreign patent documents on the Form PTO-1449.

Applicant respectfully requests that the Examiner initial and return the entire Form PTO-1449, to indicate that the information has been considered and made of record herein.

Rejections under 35 U.S.C. §112, first paragraph

Claims 1-15 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicant respectfully traverses this ground for rejection.

The amended claims are directed to a method of suppressing a respiratory syncytial virus (RSV) infection in an individual who has been exposed to RSV, the method comprising administering a composition comprising an ISS-containing polynucleotide to the respiratory tract of an individual in an amount sufficient to suppress an RSV infection. The claims further state that an RSV antigen is not administered in conjunction with administration of the composition. The amended claims are also directed to a kit for use in suppressing an RSV infection in an individual exposed to RSV, the kit comprising a composition comprising an ISS-containing polynucleotide, no RSV antigen, and instructions for administration of the composition to the respiratory tract.

As outlined in the response to the previous Office Action and as noted by the Examiner, the specification describes that "suppressing" viral infection "indicates any aspect of viral infection, such as viral replication, time course of infection, amount (titer) of virus, lesions, and/or one or more symptoms is curtailed, inhibited, or reduced (in terms of severity and/or duration)...." Page 11, lines 3-9, emphasis added. However, in the pending rejection, the Examiner states that "for the full scope of the claims to be enabled, the invention must function to suppress each of these aspects in some embodiment." Office Action, page 6, emphasis added. Applicant respectfully disagrees with this position.

The specification clearly states that suppression of a viral infection may be indicated by any one or more of a number of measured parameters and describes a variety of such parameters in the alternative which may be used to indicate suppression of a viral infection. See, for example, on page 11, lines 3-9, as quoted in the paragraph above. On page 35, at lines 2-8, the

specification states that reduction in viral titer indicates suppression of viral infection. As Applicant demonstrates, administration of ISS-containing polynucleotide at the site of RSV exposure, e.g. the respiratory tract, results in a reduction in RSV titer in the recipient of the ISS-containing polynucleotide. Therefore, Applicant submits that with a description of alternative parameters that can be used to indicate suppression of an RSV infection and with the demonstration of a reduction in RSV titer through administration of an immunomodulatory polynucleotide, the specification provides ample support to enable the claimed method of suppressing an RSV infection.

With regard to the experimental results, the Examiner states that "the working examples failed to show any significant effect on viral infection" and that "the claimed invention does not function to produce a statistically significant effect on viral titer." On page 7 of the Office Action, the Examiner states that "Applicant notes that SEQ ID NO:1 used in the examples is representative of the claimed genus. This argument if unpersuasive because, the working examples failed to show any significant effect on viral infection." The Examiner concludes that "the available evidence of record supports the unpredictability of the art by showing that the claimed invention does not function as intended." Office Action, page 7. Applicant respectfully traverses with these conclusions.

As an initial matter, at several places in the Office Action, the Examiner points to results of experiments using influenza virus exposure to support his assessment that administration of ISS oligonucleotides "fail to cause any significant reduction in viral titers compared to PBS control." Office Action, page 6. For example, at page 6, the Office Action refers to Tables 7 and 9 in Examples 4 and 5 of the specification. Applicant respectfully points out that the pending claims are directed to methods and kits involving RSV, not influenza virus, exposure.

Applicant respectfully submits that experimental results provided in the specification support suppression of RSV infection by demonstrating RSV titer reduction in response to administration of an ISS-containing polynucleotide at the site of RSV exposure. As discussed by

the Examiner at page 6 of the Office Action, Figure 1 and Table 2 in the specification show a greater than 10-fold reduction in viral titer upon administration of an ISS-containing polynucleotide. Despite this greater than 10-fold reduction in viral titer, the results in Table 2 are not quite statistically significant, as noted in the specification and by the Examiner.

Applicant has provided herein, in the form of an Applicant's Declaration, additional experimental data to support of suppression of an RSV infection with administration of an ISS-containing polynucleotide to the respiratory tract of a model animal exposed to RSV.

The Declaration provides results of an experiment performed as described in Examples 1 and 2 of the specification. In this experiment, model animals treated with a 150 microgram dose of an ISS-containing polynucleotide showed a statistically significant reduction in RSV lung titer of greater than 100-fold compared to that of animals treated with phosphate buffered saline control. Thus, this Declaration provides statistically significant evidence to support the effectiveness of the claimed method in suppressing an RSV infection and to demonstrate that the claimed invention functions as intended.

As noted above, the Examiner was unpersuaded that the ISS-containing polynucleotide SEQ ID NO:1 is representative of the claimed genus because "the working examples failed to show any significant effect on viral infection." Applicant's Declaration provides statistically significant evidence of the effectiveness of SEQ ID NO:1 in a suppression of an RSV infection. In addition, as shown in Example 2 in the specification, administration of a polynucleotide that does not contain an ISS (non-ISS, SEQ ID NO:9) resulted in the same viral titer as the administration of phosphate buffered saline control. The only difference between the effective SEQ ID NO:1 and the ineffective SEQ ID NO:9 is the presence of 5'-CG-3' sequences in SEQ ID NO:1 and not in SEQ ID NO:9.

Further, Applicant notes that the specification describes ISS-containing polynucleotides for use in the invention. See, for example, page 17, line 3 to page 20, line 24. The specification also describes how to make ISS-containing polynucleotides (for example, at page 20, line 25 to

page 24, line 28) and how to test such polynucleotides for ISS activity (for example, at page 13, lines 9-16; and page 17, lines 3-10). The specification describes methods to determine whether a given ISS-containing polynucleotide comprising the sequence 5'-C, G-3' exhibits a suppressing effect on RSV infection as claimed. See, for example, page 30, line 6 to page 35, line 28. An effective dosage that can be used for a given host and the effectiveness of a claimed ISS-containing polynucleotide with a 5'-C, G-3' sequence can be determined using that described in the specification and the knowledge of one skilled in the art.

Thus, the specification provides adequate guidance pertaining how to make and use the claimed polynucleotides comprising an ISS. Accordingly, the pending claims are in compliance with the enablement requirements.

In sum, Applicant submits that the pending claims fall within the subject matter that is enabled by the specification. Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

CONCLUSION

Applicant believes that all issues raised in the Office Action have been properly addressed in this response. Accordingly, reconsideration and allowance of the pending claims is respectfully requested. If the Examiner feels that a telephone interview would serve to facilitate resolution of any outstanding issues, the Examiner is encouraged to contact Applicant's representative at the telephone number below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this

document to **Deposit Account No. 03-1952** referencing docket no. 377882000900. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: January 14, 2003

By: _____
Karen R. Zachow
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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Please enter the following amendments without prejudice or disclaimer.

In the Claims:

Please cancel claim 7 without prejudice or disclaimer.

Please amend claims 1, 8, 9 and 11 as follows.

1. (Amended) A method of suppressing a respiratory syncytial virus (RSV) infection in an individual who has been exposed to RSV, comprising administering a composition to the respiratory tract of an individual, said composition comprising a polynucleotide comprising an immunostimulatory sequence (ISS) to said individual, wherein the ISS comprises the sequence 5'-C, G-3', wherein an RSV antigen is not administered in conjunction with administration of said composition, and wherein said composition is administered in an amount sufficient to suppress [a] an RSV infection.

8. (Amended) The method of claim [7] 1, wherein [the site of exposure is respiratory mucosa] administration is to a lung.

9. (Amended) The method of claim [7] 1, wherein [the site of exposure] administration is to the nasal passages.

11. (Amended) A kit for use in suppressing a respiratory syncytial virus (RSV) infection in an individual [infected with or] exposed to RSV, comprising:

a composition comprising a polynucleotide comprising an immunostimulatory sequence (ISS), wherein the ISS comprises the sequence 5'-C, G-3' and wherein said kit does not comprises an RSV antigen; and

instructions for administration of said composition to the respiratory tract of an individual [infected with or exposed to RSV] to suppress an RSV infection.

PATENT
Docket No. 377882000900

CERTIFICATE OF MAILING BY "FIRST CLASS MAIL"

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231, on January 14, 2003.

Rhea Amid

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Gary VAN NEST

Serial No.: 09/802,686

Filing Date: March 9, 2001

For: METHODS OF PREVENTING AND TREATING RESPIRATORY VIRAL INFECTION USING IMMUNOMODULATORY POLYNUCLEOTIDE SEQUENCES

Examiner: R. A. Schnizer

Group Art Unit: 1635

DECLARATION OF GARY VAN NEST, PH.D.
PURSUANT TO 37 C.F.R. § 1.132

Box RCE
Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

I, Gary Van Nest, Ph.D., declare as follows:

1. I currently reside at 639 Skyline Drive, Martinez, California 94553.

2. I am the inventor named in the above-referenced patent application, and am familiar with the patent specification.

3. Described herein are results from an experiment performed by me or under my direction on respiratory syncytial virus (RSV) infection. This experiment was carried out as described in Examples 1 and 2 of the patent specification using cotton rats, RSV strain A2 and

oligonucleotides SEQ ID NO:1 and SEQ ID NO:9, as described on page 38 of the patent specification.

4. Twenty cotton rats were divided into 5 groups of four animals and treated once intranasally with varying doses of an ISS-containing oligonucleotide (SEQ ID NO:1) or with controls. Three days later, each animal was inoculated intranasally with 100 median tissue culture infectious doses ($TCID_{50}$) of RSV A2. Four days after viral inoculation, each animal was sacrificed. The lungs were removed, rinsed, and viral titers determined using virus-induced cytopathic effects as an endpoint as described in Example 1 on pages 38 and 39 of the patent specification.

5. The results of this experiment are herein presented in Table 1 and Figure 1 in Exhibit A. Cotton rats, treated once intranasally with a 150 μg dose of the ISS-containing oligonucleotide, showed a reduction in RSV virus lung titers in 3 of 4 animals compared to animals treated with PBS (see Exhibit B). Rats treated with either the 50 or 450 μg dose of the ISS-containing oligonucleotide or with non-ISS oligonucleotide (SEQ ID NO:9) showed no significant reduction in viral titers following RSV infection.

6. The data indicates that administration of 150 μg of an ISS-containing oligonucleotide to the site of RSV exposure results in a statistically significant reduction in lung viral titers compared to PBS treated animals.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

January 7, 2003
Date

Gary Van Nest

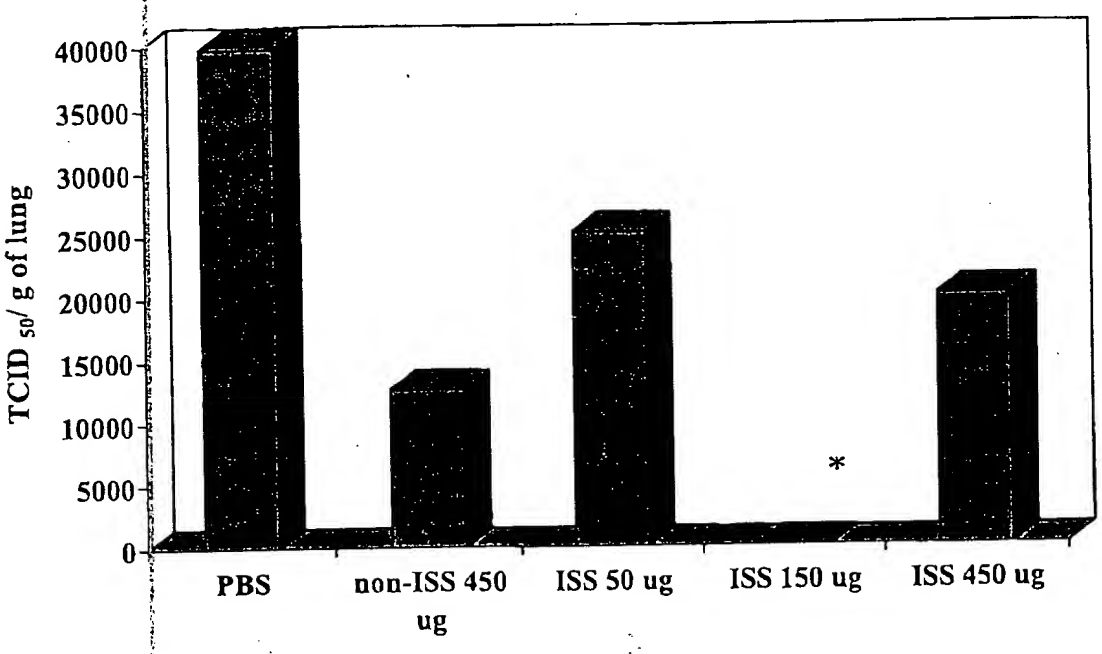
sd-123556

Table 1. RSV titers in lung

Group	Treatment	$TCID_{50}$ (log_{10}/g lung) in cotton rat no. 1	2	3	4	Mean	Std. Dev.
1	PBS	4.5	5	4	5	4.6	0.5
2	Non-ISS, 450 ug	4	4	4	4.5	4.1	0.3
3	ISS, 50 ug	5	4.5	4	4	4.4	0.5
4	ISS, 150 ug	3	4	0	0	1.8*	2.1
5	ISS, 450 ug	4	4	4.5	4.5	4.3	0.3

* p=0.05 compared to PBS, Kruskal-Wallis, nonparametric test

Figure 1.



* p=0.05 compared to PBS, Kruskal-Wallis, nonparametric test